Treating Depression: Can We Talk?

An extensive study of depressed patients, comparing the effectiveness of two forms of brief psychotherapy with drug and placebo treatments, promises to shed some light on a question rarely addressed by such research: Which approach works best for what types of depressed patients? Preliminary results from the study, directed by psychologist Irene Elkin and her colleagues at the National Institute of Mental Health (NIMH) in Rockville, Md., were presented last week in Washington, D.C., at the annual meeting of the American Psychiatric Association.

Overall, says Elkin, the "talk" therapies – cognitive behavior therapy and interpersonal therapy – alleviated depressive symptoms as well as the commonly prescribed antidepressant drug imipramine and markedly better than the pill placebo. These are "averaged" data, however, from 236 moderately to severely depressed patients treated in medical centers at George Washington University in Washington, D.C., the University of Oklahoma in Oklahoma City and the University of Pittsburgh. The success of the psychotherapies varied significantly across the three sites, notes Elkin; further analysis of the data will examine site-specific effects, such as the patient-therapist relationship and therapist skill in carrying out the assigned treatment.

The 18 psychotherapists in the study were experienced clinicians who received special training in the therapy to be performed. Cognitive behavior therapy attempts to correct distorted thinking and overly negative views of oneself, the world and the future. Interpersonal therapy focuses on developing better ways to relate to family members, coworkers and others. In both cases, weekly one-hour sessions were conducted for 12 to 16 weeks.

Imipramine and the pill placebo were dispensed weekly by experienced psychiatrists, who also provided about a half hour of support and encouragement per week.

The patients, 70 percent of whom were women, ranged in age from 21 to 60. Each patient underwent an average of 13 weeks of treatment; 162 patients completed 16 weeks of treatment. Symptom improvement was determined through the reports of patients, therapists and independent clinicians.

More than half of all patients in both the therapy and the drug groups recovered with no serious symptoms after 16 weeks, says Elkin, compared with 29 percent of the pill placebo group. The least depressed patients did surprisingly well in the pill placebo group, she adds, indicating that this approach may significantly help many moderately depressed individuals.

Severely depressed patients, on the other hand, did not respond well to the placebo condition. Those in the imipramine and interpersonal therapy groups showed the most improvement. Patients given cognitive behavior therapy displayed slightly less improvement, although not to a statistically significant degree.

In addition, says psychiatrist Stuart Sotsky of George Washington University, there are indications that certain types of depressed patients responded best to specific treatments. For example, married patients with longer episodes of moderate depression responded best to cognitive behavior therapy. Interpersonal therapy worked best with men who had relatively high levels of social functioning, he reports, and imipramine was most effective with married patients suffering from severe depression and work difficulties.

Crucial data on the maintenance of improvement during an 18-month follow-up have not yet been analyzed, says Elkin. Future studies, she explains, must also examine the role in treatment outcome played by patient personality characteristics and patient and therapist expectations and attitudes toward treatment.

"This project will be the standard against which all other psychotherapy research will be compared," says psychiatrist Jerome Frank of Johns Hopkins University in Baltimore, "although I'm somewhat pessimistic about psychotherapy research methods in general." Therapy often resembles a rhetorical attempt to influence another person's attitudes and behavior, he says, rather than a "science" that can be easily evaluated.

Researchers also need to study the outcome of therapy-drug combinations, says psychiatrist David Kupfer of the University of Pittsburgh. This approach has recently been promoted as superior to either treatment alone. A depressed patient's support from friends and family also needs to be considered over the course of recovery, asserts Kupfer.

Despite its shortcomings, psychiatrist Don R. Lipsitt of Harvard University speculates it might provide enough justification for insurance companies to limit payments for depression treatment to cheaper drug approaches. *– B. Bower*

The biochemistry of the blues

The blues take body and mind on a dance so complex that researchers have had trouble charting the steps. Now there's evidence that a brain hormone may be involved in the debilitating symptoms of both depression and the eating disorder anorexia nervosa. While the work, reported in the May 22 NEW ENGLAND JOURNAL OF MEDICINE, has no immediate therapeutic applications, according to a member of the research team it does provide "a clue to follow" in developing treatment strategies.

Since its discovery in 1981, corticotropin-releasing hormone (CRH) has been shown to produce behavioral and physiological changes characteristic of depression when injected into the brains of rats. But according to George Chrousos, who took part in the new study, levels of the hormone are difficult to measure in humans because it is contained in a small, closed circulatory system between the pituitary and the hypothalamus. So Chrousos and his colleagues at the National Institute of Mental Health (NIMH) and the National Institute of Child Health and Human Development (NICHD) in Bethesda, Md., teased apart a convoluted endocrine feedback loop to deduce elevated levels of CRH in depressives and anorexics.

CRH, produced by the hypothalamus in the brain, stimulates the pituitary gland to produce a hormone called adrenocorticotropic hormone (ACTH). That hormone "turns on" the adrenal glands' production of cortisol. Then, feeding back, high levels of cortisol act on both the pituitary and the hypothalamus to "turn off" further production of hormones. Scientists have known for decades that depressives and anorexics have a defect somewhere in the production cycle that results in abnormally high levels of cortisol.

The researchers injected CRH into their subjects and found that in depressed and anorexic patients the pituitary did not make much more ACTH in response; it "knew," through feedback, that cortisol levels were adequate. But while the levels of ACTH didn't jump, the adrenals were hyperresponsive, producing large amounts of cortisol – as they would if they were constantly stimulated by ACTH. Together, the scientists say, the findings indicate that the defect in these patients occurs before the pituitary plays its part, at the level of the hypothalamus or even before that. That would mean that the high levels of cortisol seen in depressed and anorexic patients reflect abnormally high levels of CRH.